REMARKS

Requirements for the Disclosure of Nucleotide and/or Amino Acid Sequences pursuant to 37 CFR 1.821-1.825

The Examiner has noted that the sequences disclosed in at least Figures 1-3 and 12-13 are not accompanied by SEQ ID numbers. Applicant hereby amends the Description of Figures in the specification to introduce the appropriate SEQ ID numbers.

The sequence listing has been objected to as the source organism of SEQ ID NOS:11 and 12 is listed as *Mus musculus* but SEQ ID NO:11 and 12 appear to be subsequences of SEQ ID NO:16 and 17, respectively, which are listed as human. Applicant has reviewed the last filed sequence listing which was submitted with the response dated May 16, 2005 and has noted that the source organism of SEQ ID NOs:11 and 12 is listed as *Homo sapien*. A copy of the sequence listing presently on file is attached hereto as Exhibit A.

Claim for priority under 35 U.S.C. 120

The Examiner maintains that Claims 35-44 and 46-54, which read on SEQ ID NOs: 16 or 17, have a priority date corresponding to the filing date for U.S. Serial 09/264, 527 of March 8, 1999 as the earliest priority document (U.S. Serial No. 09/244, 448, hereafter the "'448 application") discloses an amino acid sequence which has 14 fewer amino acids than SEQ ID NO:17. The Examiner argues that the priority claim should be rejected "because the instant claims are broader in scope than the disclosure of the priority application."

Applicant maintains that the disclosure of the '448 application is commensurate in scope with Claims 35-44 and 46-54. As an example, the '448 application at p. 40, lines 3-9 discloses antibodies which bind B7RP-1 as follows:

> ...B7RP1 polypeptides, fragments, variants, and/or derivatives may be used to prepare antibodies using methods known in the art. Thus, antibodies that react with ... B7RP1 polypeptides, as well as reactive fragments of such antibodies, are contemplated as within the scope of the present invention.

where the term "B7RP1 polypeptide is defined starting at p. 30, line 30 to encompass the polypeptide of SEQ ID NO:12 and all related polypeptides described herein. In addition, original Claim 13 is directed to "[a]n antibody or fragment thereof specifically binding the polypeptide of Claims 9, 10, 11 or 12" wherein Claim 12 recites in part an isolated polypeptide comprising the amino acid sequence of Figure 3A (SEQ ID NO:12) or a mature form thereof. Thus, the '448 application discloses and claims antibodies which bind B7RP1 that are within the scope of the present claims and satisfies the requirements under 35 U.S.C. 112 for B7RP1 antibodies. Applicant maintains that Claims 35-44 and 46-54 are entitled to the filing date of the '448 application.

Rejections under 35 U.S.C. 112

Claims 37-44 and 48-54 are rejected under 35 U.S.C. 112, first paragraph as allegedly failing to provide adequate written description for an antibody which binds both human (SEQ ID NO:17) and mouse (SEQ ID NO:7) B7RP-1 polypeptide (Claims 37 and claims dependent thereon). The Examiner has dismissed Applicant's arguments as not persuasive and alleges that the specification and original claims provides support for antibodies which react with human and mouse B7RP-1 polypeptides in the alternative but not support for an antibody which binds to both human and mouse B7RP-1 polypeptides. Applicant disagrees.

Applicant pointed out that support for Claims 37-44 and 48-54 was found at p. 49-50 of the specification. At p. 49, starting on line 26, it is stated that:

> A selective binding agent interacts either with CRP1 or B7RP1 and in turn regulates the binding of CRP1 to B7RP1. ... In another embodiment, the selective binding agent is an antibody. The antibody may be immunoreactive with either CRP1 or B7RP-1 and is preferably immunoreactive with B7RP-1. [Applicant's emphasis]

At p. 50, starting on line 9, it is stated that:

> CRP1 or B7RP1 polypeptides, fragments, variants, and/or derivatives may be used to prepare antibodies using methods known in the art. Thus antibodies that react with the CRP1 or B7RP1 polypeptides, as well as reactive fragments of such antibodies, are also contemplated as within the scope of the present invention. ...The antibody fragment may

> be any fragment that is reactive with CRP1 and B7RP1 polypeptides of the invention. [Applicant's emphasis]

The specification clearly states that antibodies may bind to B7RP-1, B7RP1 polypeptides or B7RP1 polypeptides of the invention. As indicated at p. 40, lines 8-12, the term "B7RP-1 polypeptide" refers to a polypeptide having the amino acid sequence of "Figure 2A (SEQ ID NO:7) and Figure 3A (SEQ ID NO:12) and all related polypeptides described herein.". The terms B7RP-1, B7RP-1 polypeptides and B7RP-1 polypeptides of the invention encompass both human and murine B7RP-1 (as well as other related polypeptides). Based on this disclosure, it is clear the Applicant contemplated and had possession of an antibody which binds to more than a single B7RP-1 polypeptide such as, for example, an antibody which binds to human B7RP-1 and mouse B7RP-1. There is nothing in the specification explicitly or implicitly disclosing an antibody that binds only human B7RP-1, or only mouse B7RP-1, or only one variant or derivative of B7RP-1 and not any other form of the polypeptide. In addition, there is no requirement for a literal recitation of an antibody which binds both human and mouse B7RP-1 polypeptides but only for a disclosure indicating that Applicant had possession of such an antibody. Applicant has clearly provided that. The Examiner has no factual or legal basis for the conclusion that there is no adequate written description for the claimed subject matter.

Claims 42 and 43 are rejected under 35 U.S.C. 112, first paragraph, as the specification allegedly fails to provide adequate written description for claim amendments that recite "an agonist antibody that increases B7RP-1 mediated immune costimulatory activity" and "an antagonist antibody that decreases B7RP-1 mediated immune costimulatory activity". The Examiner alleges that the limitations in the present claims introduce new matter. Applicant disagrees.

Support in the specification is found at, for example, p. 64, lines 18-21 where it is stated that:

> [a]gonists and antagonists include those molecules which regulate CRP1 and/or B7RP1 activity and either increase or decrease at least one activity of a CRP1 or B7RP1 protein ... . Potential polypeptide agonists and antagonists include antibodies that react with either soluble or membrane-bound forms of CRP1 or B7RP1 which comprise part or all of the extracellular domains of the said proteins. [Applicant's emphasis]

An example of an antibody which decreases B7RP1 mediated immune co-stimulation is described in Example 17 starting on p. 94 of the specification. The disclosure states that:

> B7RP-1-Fc co-stimulates T cells to proliferate in a dose-dependent fashion (Fig. 15a), and an anti-B7RP-1-Fc antibody specifically inhibits this co-stimulation dose-dependently (Fig. 15b) (p. 96, lines 20-25).

Figure 15b shows a decrease in co-stimulation of T cells with increasing concentrations of anti-B7RP1 antibody. Consequently, there is no basis whatsoever for the Examiner's statement that Claims 42 and 43 "recite limitations which were not clearly disclosed in the specification...".

Without acquiescing to the rejection and solely to advance prosecution, Applicants have amended Claims 42 and 43 to delete references to "antagonist" and "agonist" antibodies. Withdrawal of the rejection is requested.

Claims 42-44 are rejected under 35 U.S.C. 112, first paragraph, as the specification, while being enabling for an anti-B7RP1 antibody which inhibits B7RP1-induced T cell proliferation, is allegedly not enabling for a B7RP1 antibody which inhibits, increases or decreases immune costimulatory activity. Applicant has previously pointed out that the specification provides evidence that the B7RP1 protein enhances known immune disorders (rheumatoid arthritis and inflammatory bowel disease, see Examples 18 and 19) by immune costimulation. Using the disclosure of B7RP1 activity, it would be within the level of skill in the art to identify antibodies which bind to B7RP1 and either increase or decrease immune costimulation. The Examiner alleges that the argument is not persuasive because:

> The effect of administration of a polypeptide is not seen as sufficiently predictive of the effect of the corresponding antibody, as instantly claimed. ...it is not clear that reliance on the experimental observations in the results obtained using the B7RP-1 polypeptide described in the instant specification provide sufficient basis for employing the claimed antibodies for inhibiting, decreasing or increasing immune costimulatory activity. [Office Action of August 28, 2006 at p. 9]

The test for enablement is whether undue experimentation would be required by one skilled in the art, following the teachings of the specification and knowledge of the art, to carry out the claimed invention. Factors that may be considered when determining whether experimentation is undue have been previous described *In re Wands* (8 USPQ2d 1400, 1404 (Fed Cir (1988)). In particular, it has been noted in *Wands* that screening for antibodies with desired properties is to be expected and that such screening of antibodies, when routine, is not deemed to be undue experimentation.

The Examiner has not established a *prima facie* case of nonenablement. In the first instance, no evidence has been presented suggesting that one skilled in the art following the specification would need to undertake undue experimentation to identify antibodies which bind to B7RP1 and inhibit, decrease or increase immune costimulatory activity. It is alleged that the state of the art was highly unpredictable in view of Balzar et al. (J. Immunol. 157, 3250-3259 (1996)) which was cited as support for the alleged highly unpredictable art of antibody therapy. The Blazar reference describes the use of antibodies to CD80 (B7.1) and CD86 (B7.2) to block binding of these molecules to CD28 and inhibit T cell co-stimulation. It was also noted in a section of the article specifically pointed out by the Examiner (p. 3257, column 2, paragraph 1) that CD80 and CD86 antibodies gave a superior effect on graft-versus-host disease (GVHD):

> ...preliminary experiments have shown that anti-CD80 + anti-CD86 mAb given in the same dose and schedule as hCTLA4Ig, were significantly more effective in preventing GVHD lethality due to either CD4+ or CD8+ T cells (data not shown).

Balzar et al. suggests that the degree to which a molecule can block co-stimulation and achieve a therapeutic effect can depend on a number of factors such as tissue distribution. half-life, affinity and avidity. However, there is no indication whatsoever in the reference that the observed variability in these factors would cause difficulty in obtaining a B7 inhibitor which could block costimulation. It should also be noted that, according to Balzar et al., antibodies to CD80 and CD86 are able to regulate immune response as evidenced by their effects on GVHD lethality.

The Examiner's arguments with respect to alleged lack of enablement are moot in view of Example 17 of the specification which shows inhibition of T-cell costimulation by either rabbit anti-mouse B7RP-1 polyclonal antibodies or rat anti-mouse B7RP1 monoclonal antibodies. The specification provides a working example of the subject matter in Claims 42-44 and as a result enables the claims. It is requested that the rejection be withdrawn.

Without acquiescing to the rejection and solely to advance prosecution, Applicant has amended Claim 42-44 to recite "T cell costimulatory activity". Support for this amendment is found at p. 94, lines 2-3 of the specification.

Provisional rejection for obviousness-type double patenting

Claims 33-54 are provisionally rejected under obviousness-type double patenting as being unpatentable over Claims 13-18 of co-pending U.S. Application Serial No. 11/359,254. The Examiner argues that the claims are not patentably distinct because they directed to "the same or nearly the same antibodies to B7RP-1 polypeptide."

U.S. Serial No. 11/359,254 was filed as a divisional application of U.S. Serial No. 09/728,420 on February 21, 2006. In a preliminary amendment filed on February 21, 2006, Applicants elected to prosecute Claims 32-34 and 36-38 directed to a method of decreasing IgE production and cancelled Claims 1-31, 35 and 39-42, thus rendering the rejection moot.

CONCLUSION

Claims 33-54 are in condition for allowance and an early notice thereof is solicited.

The Commissioner is hereby authorized to charge any necessary fees or credit any overpayments to Deposit Account No. 01-0519.

Respectfully submitted,

Robert B. Winter
Attorney/Agent for Applicant(s)
Registration No.: 34,458
Phone: (805) 447-2425
Date: October 15, 2007

Please send all future correspondence to:

21069

US Patent Operations/RBW
Dept. 4300, M/S 28-2-C
AMGEN INC.
One Amgen Center Drive
Thousand Oaks, California 91320-1799